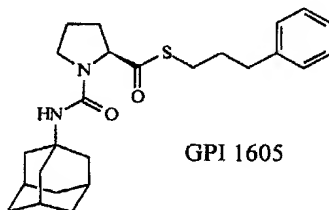


## DETAILED DESCRIPTION OF THE INVENTION

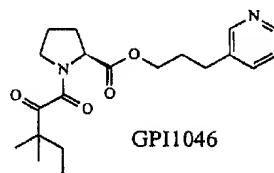
### Definitions

"Eye" refers to the anatomical structure responsible for vision in humans and other animals, and encompasses the following anatomical structures, without limitation: lens, vitreous body, ciliary body, posterior chamber, anterior chamber, pupil, cornea, iris, canal of Schlemm, zonules of Zinn, limbus, conjunctiva, choroid, retina, central vessels of the retina, optic nerve, fovea centralis, macula lutea, and sclera.

"GPI 1605" refers a compound of formula

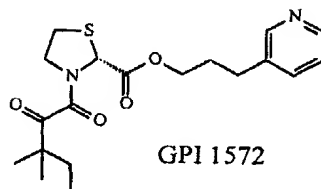


"GPI 1046" refers to 3-(3-pyridyl)-1-propyl (2s)-1-(3,3-dimethyl-1,2-dioxopentyl)-2-pyrrolidine-carboxylate, a compound of formula



In a preferred embodiment of the compounds of formula II, the heterocyclic ester or amide is the compound GPI 1572, of the formula

5



In a particularly preferred embodiment of formula  
10 II compounds:

A is  $\text{CH}_2$ ;

B is  $\text{CH}_2$  or S;

C is  $\text{CH}_2$  or NH;

$\text{R}_1$  is selected from the group consisting of 3-  
15 phenylpropyl and 3-(3-pyridyl)propyl; and

$\text{R}_2$  is selected from the group consisting of 1,1-dimethylpropyl, cyclohexyl, and tert-butyl.

Specific examples of this embodiment are presented in TABLE I.

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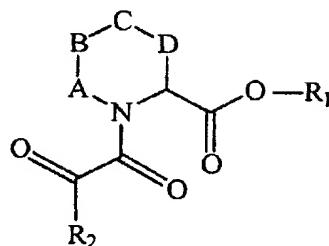
**TABLE I**

No.	A	B	C	$\text{R}_1$	$\text{R}_2$
1	$\text{CH}_2$	S	$\text{CH}_2$	3-phenylpropyl	1,1-dimethylpropyl
2	$\text{CH}_2$	S	$\text{CH}_2$	3-(3-pyridyl)propyl	1,1-dimethylpropyl
3	$\text{CH}_2$	S	$\text{CH}_2$	3-phenylpropyl	cyclohexyl
4	$\text{CH}_2$	S	$\text{CH}_2$	3-phenylpropyl	tert-butyl
5	$\text{CH}_2$	$\text{CH}_2$	NH	3-phenylpropyl	1,1-dimethylpropyl
6	$\text{CH}_2$	$\text{CH}_2$	NH	3-phenylpropyl	cyclohexyl
7	$\text{CH}_2$	$\text{CH}_2$	NH	3-phenylpropyl	tert-butyl

FORMULA III

The heterocyclic ester or amide may also be a compound of formula III

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III

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or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

A, B, C and D are independently CH<sub>2</sub>, O, S, SO, SO<sub>2</sub>, NH or NR<sub>1</sub>;

15

R<sub>1</sub> is C<sub>1</sub>-C<sub>5</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>5</sub> straight or branched chain alkenyl, which is substituted with one or more substituent(s) independently selected from the group consisting of (Ar<sub>1</sub>)<sub>n</sub> and C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl substituted with (Ar<sub>1</sub>)<sub>n</sub>;

20

n is 1 or 2;

R<sub>2</sub> is either C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>5</sub>-C<sub>7</sub> cycloalkenyl, or Ar<sub>1</sub>; and

25

Ar<sub>1</sub> is an alicyclic or aromatic, mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either unsubstituted or substituted with one

**Efficacy of representative compounds from  
different immunophilin ligand series  
in protecting retinal ganglion cell axons from  
degeneration following optic nerve transection**

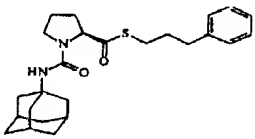
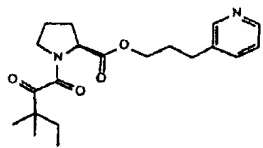
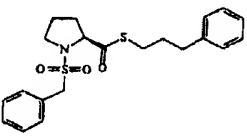
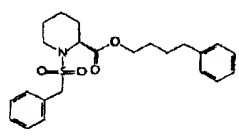
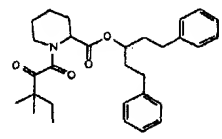
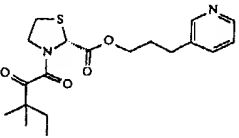
Compound	Structure	Comments	RT97+RGC axon density 14 days after ON transection (% ON axons rescued)
B		Adamantyl Thioester of urea Ki rotamase = 149 nM Clearance=? $\mu$ l/min	100.0% $\pm$ 5.2% SEM
A GPI 1046		Ester Ki rotamase = 7.5nM Clearance=63.8 $\mu$ l/min	60.5% $\pm$ 3.9 SEM
C		Sulfonamide Ki rotamase = 107nM Clearance= 31.1 $\mu$ l/min	60.4% $\pm$ 3.1 % SEM
D		Pipecolic sulfonamide Ki rotamase= nM Clearance= $\mu$ l/min	58.4% $\pm$ 6.4% SEM
E		Ester of pipecolic acid Ki rotamase = 20 nM Clearance = 41.8 $\mu$ l/min	56.6% $\pm$ 9.4% SEM
F		Proline heterocycle Analog of GPI 1046 Ki rotamase = 272 nM Clearance=? $\mu$ l/min	55.1% $\pm$ 5.9% SEM

TABLE V